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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,787	06/26/2001	Carl Nelson Skold		4399

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CARL SKOLD
2487 DELL AVENUE
MOUNTAIN VIEW, CA 94043

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,787	SKOLD, CARL NELSON	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *20-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) ~~20-52~~ 1-53 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry & Claim Status

The amendment filed on November 21, 2003 has been acknowledged and entered.

Claims 1-19, 53 are examined. Claims 20-52 are withdrawn from further consideration.

Withdrawn Rejection(s)

Rejection under 35 USC 112, 2nd paragraph in the previous office action is withdrawn herein.

Maintained Rejection(s)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 9, 11, 14, 19, 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Molday (US 4,452,773).

Molday teaches a method of separating a target material from a suspension or dispersion, said method comprising the steps of: combining magnetizable particles composed of magnetic iron oxide coated with a polysaccharide, preferably dextran, or a derivative thereof having pendant functional groups with a suspension containing a target binding material for said target material to bind to said magnetizable particles;

and applying a magnetic field to said suspension or dispersion to separate the magnetizable particles and target material. The target binding material is an antigen, antibody, or nucleic acid. The target material is a biological material. The magnetic particles have a particle size of about 100 to 700 Angstrom. (see col. 3, lines 14-22). The purified complex of magnetizable particles bound to said target material is dissociated and said magnetic particles are removed by magnetic means to provide substantially pure preparation of said target material. (see col. 4, lines 31-38). The magnetizable metal oxide is an iron oxide (see col. 3, lines 1-2). The magnetizable particles are produced by treating with a base- NH4OH. (see col. 8, lines 38-40). The pendant functional group of the polysaccharide is an aldehyde group (see col. 54-56). The polysaccharide is dextran. (see col. 4, lines 10-50). Molday teaches the same method for making particles as in Example 1 of the specification of the present invention. The method comprises preparing a solution by diluting ferric chloride and ferrous chloride tetrahydrate were added dropwise with agitation over a period to a solution containing concentrated ammonium hydroxide in a water bath. Aggregates were removed by 3 cycles of centrifugation in a low-speed clinical centrifuge for 5 minutes. The ferromagnetic iron-dextran particles were separated from unbound dextran by gel filtration chromatography. Five milliliters of the reaction mixture were applied to a 2.5 X 33 cm column and eluted with sodium acetate, sodium chloride. The purified ferromagnetic iron-dextran particles were collected. Since Molday teaches the same method of making colloidal aggregates of magnetizable iron oxide particles,

Molday's magnetizable particles are formed of particles of crystallites of magnetizable metal oxide. (see col. 8, lines 31-50).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Molday (US 4,452,773) further in view of Chagnon et al. (US 4,628,037).

Molday has been discussed above.

However, Molday fails to teach that the magnetizable particles are formed of particles of crystallites of a magnetizable metal oxide; and a mass of crystallites having a particles size of about 3 nm to about 25 nm. Molday also fails to teach that the crystallites of the magnetizable metal oxide include a coating of an organosilane bonded directly to the particles of the crystallites and wherein said coating of polysaccharide derivative is bonded to said organosilane.

Chagnon teaches magnetic particles useful in biological applications involving the separation of molecules. The magnetic particles have a metal oxide core composed of a cluster of ferromagnetic crystals of an iron oxide. (see col. 7, lines 22-30). The ferromagnetism is defined as that magnetic behavior exhibited by iron oxides with crystal size greater than about 500 Angstrom. The method of preparing the magnetic particles comprises precipitating metal salts in a base to form fine magnetic metal oxide

crystals, redispersing, washing the crystals in water and in an electrolyte. The magnetic particles comprise a magnetic metal oxide core generally surrounded by an adsorptively or covalently bound organosilane coat to which a wide variety of bioaffinity adsorbents can be covalently bonded through selected coupling chemistries. The coupling chemistries include gluteraldehyde couplings; carbodimide, diazotization. (see col. 9, lines 3-12).

It would have been obvious to one of ordinary skills in the art to use clusters of ferromagnetic crystals of an iron oxide as taught by Chagnon in the method of producing the magnetic particles discussed by Molday since Molday's particles derived from iron oxide. Furthermore, it would have been obvious to one of ordinary skills in the art to add to the organosilane coating as taught by Chagnon the polysaccharide coating as taught by Molday because the hydroxyl group in polysaccharide forms a stable bond directly to the silane group. Regarding claim 52, it would have been obvious to one of ordinary skills in the art to produce a kit comprising the components for performing the combined method of Molday and Chagnon for economic convenience.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Molday in view of Niswender (US 4,048,298).

Molday has been discussed above.

However, Molday fails to teach the pendant functional group of polysaccharide is a carboxyl group attached to polysaccharide through a linker having at least one heteroatom for every three-carbon atom in the linker; the heteroatom is Oxygen; the linker is derived from ethylene glycol, an oligoethylene glycol or a polyethylene glycol.

Niswender teaches a polymeric carrier with a suitable reactive group. The reactive groups are carboxyl, hydroxyl and primary or secondary amine groups. The polymeric material is polysaccharides, dextrin. The reactive group can be crosslinked by inclusion of a substantial amount of a polyethylenically unsaturated monomer, such as ethylene glycol dimethacrylate.(see col. 4, lines 5-45).

It would have been obvious to one of ordinary skills in the art to attach carboxyl group to polysaccharide via an ethylene glycol linker as taught by Niswender to form a polymeric coating on the magnetizable particles of Molday since these polymeric coatings are used for attaching ligands/antibody to detect target analyte in assay.

Response to Arguments

Applicant's arguments filed November 21, 2003 have been fully considered but they are not persuasive.

Applicant submits that the method of making the magnetizable particle in Molday is different from that of the present invention. Molday's method includes preparing a mixture of ferrous and ferric salts with a coating material such as dextran before being added to the base, and therefore the magnetite (Fe3O4) is precipitated in the presence of the coating material while in the method of the present invention, ferric and ferrious salts are not mixed with any coating material, and thus magnetite is precipitated in the complete absence of any coating material. Applicant also asserts that in the absence of dextran, there is no coating on the crystallite. Therefore, the crystallites can directly contact one another to form aggregates. In Molday's invention, magnetite is precipitated in the presence of dextran. The particles of his invention are produced directly in his

reaction mixture, with no additional treatment steps. Each crystallite is coated with dextran. Applicant also points out that Molday states (col. 3, line 16) that his particles do not aggregate; Regarding the nature of the core, applicant argues that Molday teaches the preparation and use of particle with an electron dense core of 10-20 nm. The size of this core is consistent with the size of a single crystallite of magnetite prepared by precipitation of mixed iron salts with ammonia, as noted in the paper by Jolivet and Tronc where a particular preparation had an average crystallite diameter of 9 nm. Applicant also states that since Molday makes no comment about the presence of multiple objects in the electron dense core of his particle, hence we may presume that the core is a single object, a single crystallite. Thus, it is different than the core of the present invention, which has its core as an aggregate of crystallites. Applicant also argues that the nature of mineral in the core of Molday is different from that of the present invention. Molday teaches using Fe3O4 in the core. The iron oxide in the core of the present invention is not Fe3O4. Furthermore, Applicant distinguishes the size of the particle in Molday from that of the present invention. Molday uses a particle with a diameter of 10-70 nm whereas the particles of the applicant's invention are much larger.

Since the claims contain an opening language, the method of forming the particles can contain additional reagents such as dextran. However, the steps of the method in Molday are the same as those in the method of the present invention. Thus, the end product would be the same. The fact that the magnetite in Molday precipitates in the presence of dextran interferes with the formation of crystallite aggregates is not proven. Rather, it is just an assertion by applicants. The paper by Jolivet and Tronc

attached by applicant fails to mention or prove that dextran or any coating material interferes with the formation of crystallite aggregates. Furthermore, the claims require that the particles comprises an aggregate of crystallite and a coating on such aggregate. Thus, Molday has a dextran (coating) on the crystallites, which are aggregates. These crystallites must aggregate to form a magnetic particle. Whether dextran coats single crystallites, as asserted by applicant, or crystallite aggregates, the requirement limitation –a coating on said aggregates-- recited in the claim is met by Molday's particle. In column 3, line 16, Molday teaches that his "particles" do not aggregate. Molday is [redacted] referring to the coated particles not being aggregated, not the crystallites of the particle. This is different than the aggregation of crystallites of the particles. The magnetite crystallites need to clump together in order to form a particle. Thus, aggregation of the crystallites must take place in order to form a particle.

Regarding the distinction between the nature of the core in Molday and the present invention mentioned by Applicant, Molday has a core of 10-20 nm which is not any close to the average size, 9 nm, of the single crystallite core mentioned in by Jolivet and Tronc. Although Molday makes no comment about the presence of multiple objects in the electron dense core of his particle, it does not mean that the core of his particle is a single crystallite. It is just a presumption.

Regarding the nature of the mineral in the core in Molday and the present invention, since the nature of the mineral in the core required by the present invention is not recited in the claim, limitation in the specification is not read into the claim. The claim only requires a magnetizable particle.

Regarding the size of the magnetizable particle, the diameter range of the magnetizable particle in Molday (10-70 nm) falls within the range of the required diameter of the magnetizable particle in the recited claims, which is between 50-500 nm.

Remarks

Claims 10, 12, 18 are free of prior arts.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
April 9, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641